04

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GNT pathology cases file
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Pathology

Diarrhea

439

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- Important
- Doctor's note
- Extra info
- Main text
- ★ Male's slide
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اللهم لا سهل الا ماجعلته سهلا و انت تجعل الحزن إذا شئت سهلا

Revised & Approved

Bassam Alasmari
Rania Almutiri

Objective

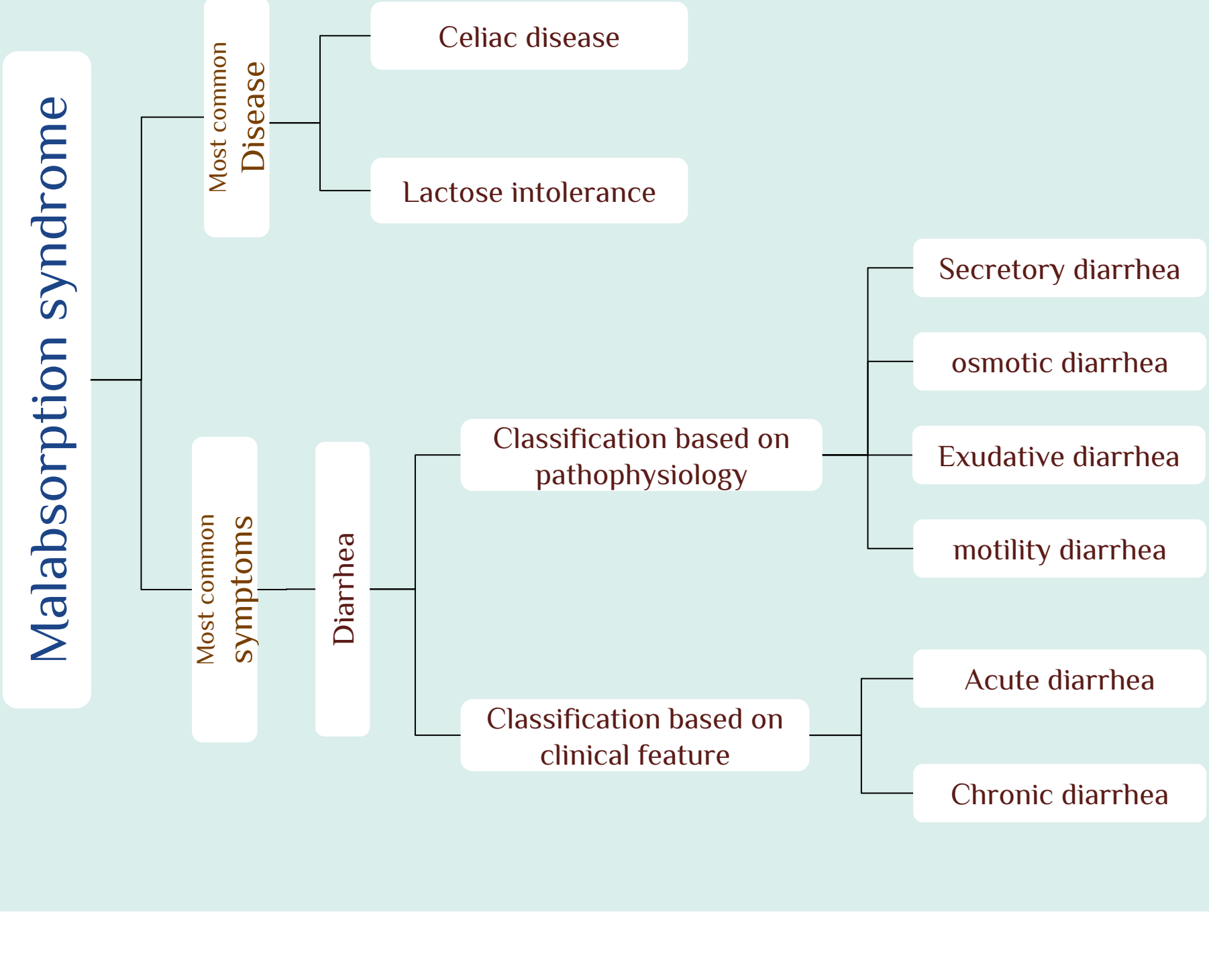
01 Understand the physiology of fluid in small intestine

02 Define diarrhea

03 Understand the four categories of diarrheal diseases, and list the major causes in each category.

04 List the causes of acute and chronic diarrhea

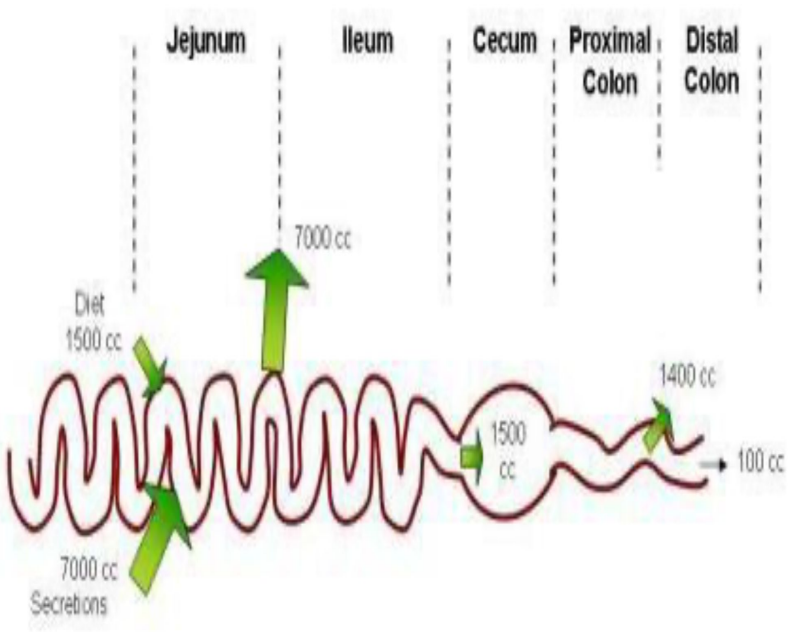
Overview



Physiology of Fluid and small intestine

- Most of the fluid is going to be absorbed in the jejunum & ileum
- In the large bowel, 1400 cc of fluid is absorbed and only 100 cc will be excreted.

Approximately 8500 mL of fluid flow into the intestine daily :
1- from diet (1500mL).
2- Secretions (7000mL), EX (salivary, gastric, biliary, pancreatic, intestinal secretions).
3- Approximately (7000 mL) will be absorbed in the small intestines (most of the volume will be absorbed in the small intestines due to weaker tight junctions between enterocytes).
4- Approximately (1500 mL) cross the ileocecal valve.
5- The colon reabsorbed most of this fluid most of the fluid (1400 mL, but less than small intestines due to stronger tight junctions).
6- Finally, only (100mL) lost in the stool



Diarrhea

Definition (World Health Organization)

- 3 or more loose or liquid stools per day.
- Abnormally high fluid content of stool ⟶ 200-300 gm/day (more than 250 g of stool per day) (normally 100)

Why important?

- The **loss of fluids** through diarrhea ⟶ can cause **dehydration** and **electrolyte imbalances**
-
- Easy to treat but if untreated, may lead to death especially in children

More than 70 % of almost 11 million child deaths every year are attributable to 6 causes:

1. **Diarrhea**
2. Malaria
3. lack of oxygen at birth
4. Pneumonia
5. preterm delivery
6. neonatal infection

Fecal osmolarity

only found in the girl's slides

- As stool leaves the colon, fecal osmolality is equal to the serum osmolality i.e. 290 mosm/kg
- Under normal circumstances, the major osmoles are Na+, K+, Cl−, and HCO −3
- **Stool osmotic gap** =Stool osmolality - 2 x (stool Na + stool K)
- **Normal fecal fluid values**: Osmolality: ~290 mOsm/kg , Na+: ~30 mmol/L , K+: ~75 mmol/L

Stool osmotic gap

Fecal Osmotic Gap
290 mosm/Kg H_2O-2([Na^+])+[K^+])

- Is a calculation performed to distinguish among different causes of diarrhea (distinguishes secretory from osmotic diarrhea)
- A normal gap is between 50 and 100 mosm/kg
- A **low stool osmotic gap** (<50 mosm/kg) can imply secretory diarrhea
- A **high gap** (>125 mosm/kg) can imply osmotic diarrhea
- The reason for this is that secreted sodium and potassium ions make up a greater percentage of the stool osmolality in secretory diarrhea, whereas in osmotic diarrhea, molecules such as unabsorbed carbohydrates are more significant contributors to stool osmolality.

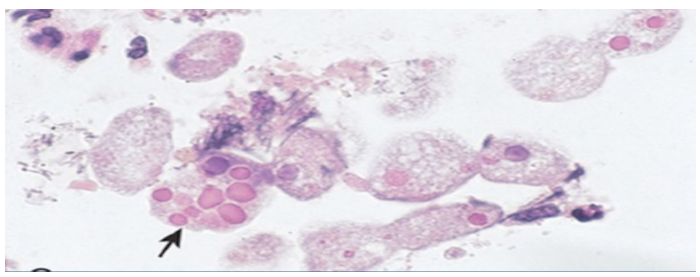
Classifications of diarrhea

1. Secretory Diarrhea
2. Osmotic Diarrhea
3. Exudative Diarrhea
4. Motility-related Diarrhea

In osmotic diarrhea: large amounts of molecules aren't absorbed. These molecules will produce osmotic pressure on the wall of the intestine so large amounts of H2O will be retained in the colon and & pass out of the intestine . This is osmotic diarrhea which occurs in malabsorption where there's no proper absorption of carbohydrates or other food nutrients (as in lactose intolerance & celiac disease)

Secretory diarrhea : the problem is in the intestine (intestinal wall), there's infection by virus or bacteria which ask the intestine to poor out fluid (fluid rich in Na and K) when we calculate this gap it will be low (>50)

	Secretory	Osmotic
Definition	❖ There is an **increase in the active secretion** of **water** and **electrolytes** ❖ Enterotoxins stimulate Cl-channels regulated by cAMP and cGMP	❖ Excess amount of **poorly absorbed substances that exert osmotic effect** , so water is drawn into the bowels causing diarrhea into bowels causing diarrhea ❖ Doesn't cause inflammation in bowel mucosa
Stool output	❖ High stool output (High-volume diarrhea) ❖ **Loss of isotonic fluid**	❖ Stool output is usually not massive ❖ Osmotically active substance is drawing **hypotonic** salt solution out of bowel
Fasting effect	**Lack of response** (even if the patient reduces food intake he will still have diarrhea)	**improve the condition**
Stool osmotic gap	Stool osmotic gap is normal or **low** < 100 mOsm/kg	Stool osmotic gap is **high** > 125 mOsm/kg (loss of hypotonic fluid)
★ Causes	❖ The most common cause of this type of diarrhea is a bacterial toxin : (enterotoxins) (E. coli, Vibrio cholera) that stimulates the secretion of anions. May lead to life threatening fluid loss , Bacteria toxin will stimulate secretion of small intestine only No RBC NO inflammation Other causes: ❖ Also seen in **neuroendocrine tumours** : (carcinoid tumor, gastrinomas with normal osmotic gap) ❖ **Enteropathogenic virus** : **rotavirus** and norwalk virus ❖ **Rectal villous adenoma** ❖ **Laxatives**: Mechanisms melanosis coli with use of phenanthrene laxatives	❖ **Malabsorption** in which the nutrients are left in the lumen to pull in water : **lactose intolerance**, chronic pancreatitis, celiac disease (associated with steatorrhea) ❖ **Osmotic laxatives (treat constipation) :** e.g. Lactulose (non-absorbable sugar) ❖ poorly absorbed Hexitols : sorbitol, mannitol, xylitol) ❖ Disaccharidase deficiency ❖ Pancreatitis giardiasis ❖ **Ingestion of poorly absorbable solutes**
SCREENING TESTS	Stool osmotic gap < 50 mOsm/kg Fecal smear for leukocytes: negative because there no inflammation	Stool osmotic gap > 125 mOsm/kg Fecal smear for leukocytes:negative

	Exudative (inflammatory) Diarrhea	Motility-related Diarrhea
Definition	Results from the outpouring of blood protein, or mucus from an inflamed or ulcerated mucosa	Caused by the rapid movement of food through the intestines (hypermotility).
Stool output	**Bacterial dysentery diarrhea** with **blood** and **pus** in the stool	-
Fating	Persists on fasting	-
Causes	❖ **Inflammatory bowel diseases (**crohn's disease & ulcerative colitis**).** ❖ **Invasive infections** e.g E. **coli**, Clostridium difficile and Shigella ❖ Some bacterial infections cause damage by invasion of the mucosa. Many cause (**bacterial dysentery**) The main organisms of bacterial dysentery are: ❖ **Campylobacter** invades mucosa in the jejunum, ileum and colon, causing ulceration and acute inflammation. ❖ Salmonella typhi, S. paratyphi A, B, and C ❖ Shigella infections are mainly seen in young children. ❖ **Enteroinvasive and enterohemorrhagic E. coli** ❖ Entamoeba histolytica, can cause liver amebic abscess 	❖ Irritable bowel syndrome (IBS): a motor disorder that causes abdominal pain and altered bowel habits with diarrhea predominating ❖ Increased serotonin: **carcinoid syndrome** : Serotonin increases bowel motility No inflammation in bowel mucosa ❖ Other causes : 1. **Diabetic diarrhoea** 2. **hyperthyroid diarrhoea** ❖ Carcinoid syndrome : disease of neuroendocrine cell that produce 5-HT, this substance increases bowel motility → opening of bowel frequently → loss of fluid (diarrhea)
Screening test	Fecal smear for leukocytes: **positive** in most cases Stool culture and for O&P (Ova and parasites)	Increased 5-HIAA (5-hydroxyindoleacetic acid)

Classifications of diarrhea

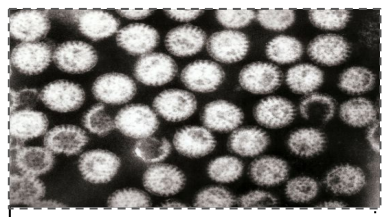
According to duration

1. Acute → if 2 weeks.
2. Persistent → if 2 to 4 weeks.
3. Chronic → if 4 weeks in duration.

Acute diarrhea

Etiology

- **Infections**: Approximately 80% of acute diarrheas (viruses, bacteria, helminths, and protozoa(amoeba) .
- **Viral gastroenteritis** : viral infection of the stomach and the small intestine is the **most common** cause of acute diarrhea worldwide.
- **Rotavirus**
  - Most common cause of Severe childhood diarrhea , diarrhea related deaths worldwide.
  - 40% of hospitalizations from diarrhea in children under 5.
  - 50% of acute diarrhea in infants.
- Preformed toxin, enterotoxin, cytotoxic or invasive.
- **Food poisoning** (Preformed enterotoxin, usually caused by staph.)
- **Drugs**: antibiotic, NSAID, anti acid , bronchodilators, antiarrhythmics.
- **Others**: occlusive colitis, ischemia, toxin (insecticides).



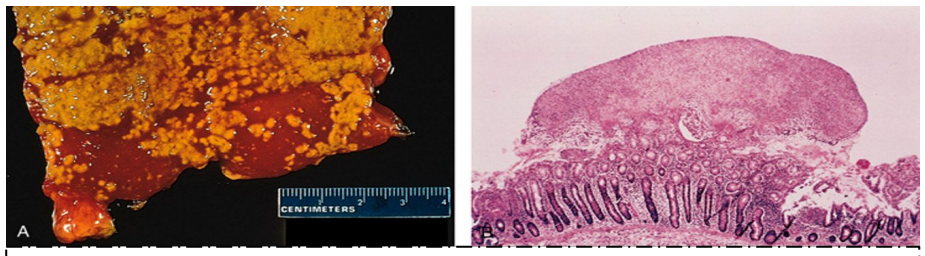
Rotavirus

Antibiotic associated diarrhea

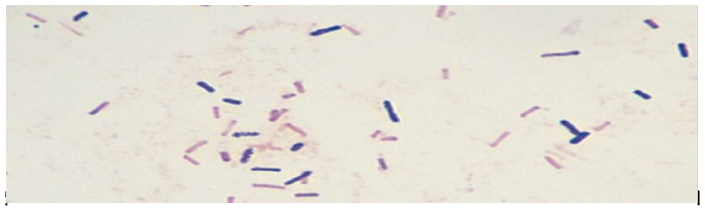
- Diarrhea occurs in 20% of patients receiving broad-spectrum antibiotics; about 20% of these diarrheas are due to Clostridium difficile.
- Leading to pseudomembranous colitis.
- Broad spectrum antibiotics kill normal flora. Among the normal flora there's few amounts of clostridium difficile but they're resistant to antibiotics leading to injury of intestinal wall & pseudomembranous colitis

Clinical Features

- Person become dehydrated with electrolyte disturbance and low bicarbonate in blood.
- Mild self limited, need rehydration.



Pseudomembranous colitis



Clostridium species
Gram-positive rods

Evaluatory test

Fecal leukocytes	
Non present	Present
Non-Inflammatory diarrhea	Inflammatory diarrhea
Suggests a small bowel source or colon but **without** mucosal injury. E.g : cholera	Suggests colonic **mucosa damage** caused by invasion: ❖ Shigellosis, Salmonellosis, Campylobacter or Yersinia infection, amebiasis). ❖ Toxin (C difficile, E coli O157:H7). ❖ Inflammatory bowel diseases.

Chronic diarrhea

Etiology

❖ **Infection:**

➢ **Giardia lamblia** (protozoa, unicellular, lives in the intestine, has 2 nuclei & flagella).

➢ **AIDS** often have chronic infections of their intestines that cause diarrhea.

❖ **Post-infectious:** Following acute viral, bacterial or parasitic infections (during regeneration and repair of intestinal wall) .

❖ **Malabsorption**

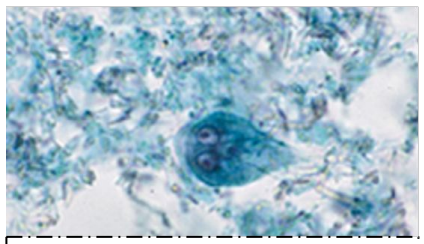
❖ **Inflammatory bowel disease (IBD)** e.g, crohn's disease & ulcerative colitis

❖ **Endocrine diseases:** e.g. carcinoid, gastrinoma.

❖ **Colon cancer** (villous adenoma)

❖ **Irritable bowel syndrome** (high motility bowel)

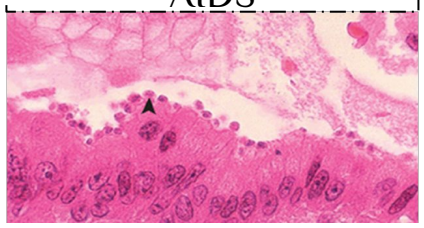
❖ *Most of the causes of chronic diarrhea are <u>noninfectious</u>.*



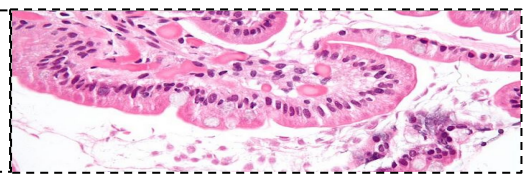
Giardia lamblia

They both cover the mucosa of the bowel and prevent the absorption

Cryptosporidiosis in AIDS



Parasitic and protozoal infections affect over half of the world's population on a chronic or recurrent basis. ★



Complications

Fluid loss	→	Dehydration
Electrolytes loss	→	Electrolytes imbalance
Low Sodium bicarbonate in blood	→	Metabolic acidosis
If persistent	→	malnutrition (iron deficiency anaemia, vitamins C & D deficiencies)

Evaluatory test

<table>
<tr><th colspan="3">Stool analysis ova, parasites</th></tr>
<tr><td>+Ve</td><td colspan="2">-Ve</td></tr>
<tr><td rowspan="2">Infection</td><td colspan="2">Stool fat test (normal <20%)</td></tr>
<tr><td>-Ve</td><td>+Ve</td></tr>
<tr><td></td><td>Secretory, Non infectious and Inflammatory diarrhea</td><td>Malabsorption
If malabsorption is +ve do:
❖ Quantitative stool for fat:
➢ Best screening test
➢ 72-hour collection of stool
➢ Positive if test >7g of fat/24 hours
❖ Serum Anti-tissue transglutaminase antibodies.
❖ Anti-endomysial IgA antibodies.
❖ Antigliadin antibodies to check for celiac disease.
❖ Duodenal biopsy</td></tr>
</table>

Signs of dehydration

Early signs	Mature signs
Fatigue	Heartburn
Anxiety	Joint pain
Irritability	Back pain
Depression	Migraines
Cravings	Fibromyalgia “bone & muscle pain “
Cramps	Constipation
Headaches	Colitis

Summary

	Secretory	Osmotic	Exudative	Motility-related
Osmotic gap	Normal <100 mosm/kg	High >125		
Fasting effect	No response	Fasting helps	Persists on fasting	
Stool	High stool output	Not massive	Blood and pus in stool	
Causes	Increased secretion due to: - Bacterial toxin (E. coli, cholera) - Zollinger ellison tumors	Poorly absorbed substance that exert osmotic effect. 1- Malabsorption 2- laxatives	Outpouring of blood or mucus from inflamed or ulcerated mucosa. 1- inflammatory bowel disease 2- invasive infection 3- colon cancer	Rapid movement of food through intestine - IBS -Diabetic diarrhea - Hyperthyroid diarrhea

Acute	Chronic
- Infections: viral gastroenteritis (rotavirus) - Food poisoning - Drugs - Antibiotic-Associated Diarrhea: Clostridium difficile	- Infection: Giardia lamblia, AIDS -> cause other infections that cause diarrhea (Aids have low immunity) - Post-infectious why? Malabsorption lactose intolerance - Malabsorption - IBD - Endocrine disease - Colon cancer - IBS

QUIZ!

MCQs

01 | Fecal smear for leukocytes is positive for which type of diarrhea :			
A) Secretory	B) Osmotic	C) Exudative	D) Motility related
02 | Motility related diarrhea usually ASSOCIATED with :			
A)Inflammatory bowel diseases	B)Irritable bowel syndrome (IBS)	C)Malabsorption	D) Entamoeba histolytica
03 | Which type of diarrhea associated with high stool osmotic gap :			
A) Secretory	B)Exudative	C) Motility related	D) Osmotic
04 | Carcinoid syndrome lead to Increase in the serotonin level in which type of diarrhea :			
A)Secretory	B)Osmotic	C)Exudative	D)Motility related
05 | A 4.5-month-old baby girl presented to hospital with a 2-day history of watery diarrhea and fever.Which of the following microorganisms is the most likely cause of diarrhea ;			
A) shigella	B) salmonella	C) Rotavirus	D) E. coli
06 | Which of these sentences is true about steatorrhoea :			
A) Is cause by the malabsorption of proteins, producing a pale, foul smelling stool.	B) Passage of soft, greenish, greasy stool	C) Characteristically floats on water	D) Is caused by the malabsorption of fat, producing brown, fruity smelling stool
7 | All of the following are causes of acute diarrhea except :			
A) Viral gastroenteritis	B) Food poisoning	C) Inflammatory bowel disease	D) Antibiotic Associated Diarrhea
8 | which one of the following organisms may cause secretory diarrhea :			
A) Cholera	B) gonorrhea	C) s.aureus	D) l.monocytogenes
9 | Which of these is an Mature sign of dehydration :			
A) Heartburn	B) Fatigue	C) Depression	D) Headaches

MCQs Answer key	01	02	03	04	05	06	07	08	09
	C	B	D	D	C	C	C	A	A

" اللهم علمنا ماينفعنا ، وانفعنا بما علمتنا وزدنا علما يارب العالمين "

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Hamad Almousa

Fatimah Alhilal

Team members

- Hadi Alhemsi
- Abdulrahman Almebki
- Ghada Alabdi
- Khalid Alsubaie
- Hassan alshurafa
- Mariam Alruhaimi
- Abdulrahman Barashid
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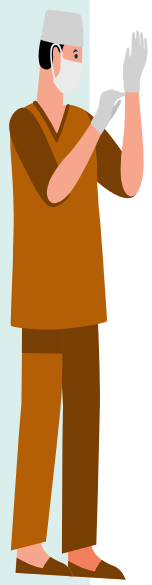

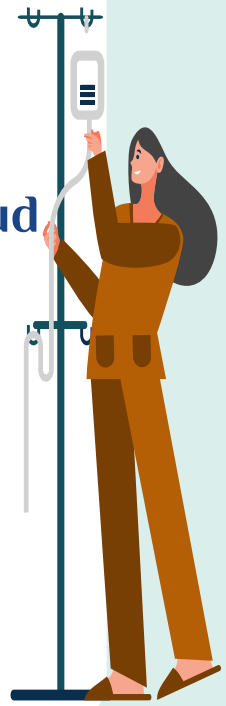

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- Reviser

Contact us through :
Pathology439@Gmail.com